

REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS AND AMENDMENTS

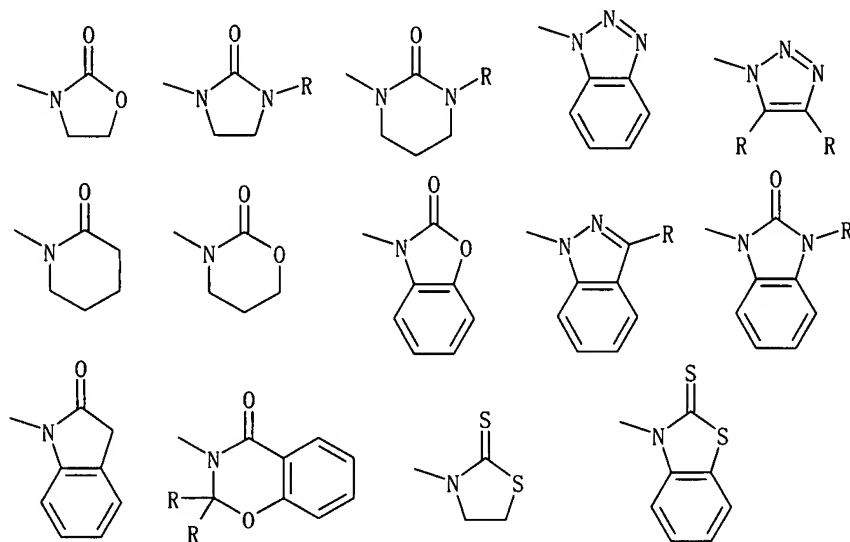
Claims 1-7 were pending in this application when last examined.

Claims 1-7 were examined on the merits and rejected.

Claim 6 is amended to delete "hydrogen atom" from the definition of R^1 . Claim 6 is also amended to separately define R^2 in conformance with the definition of R^2 in claim 6 as filed.

Claim 8 is newly added and is a combination of claims 1 and 4. Thus, support can be found in these claims.

Claim 9 is newly added. Support for this claim can be found in claim 6 as filed and the specific R^d disclosed on page 24, lines 1-6, *i.e.*,



, of the specification as filed.

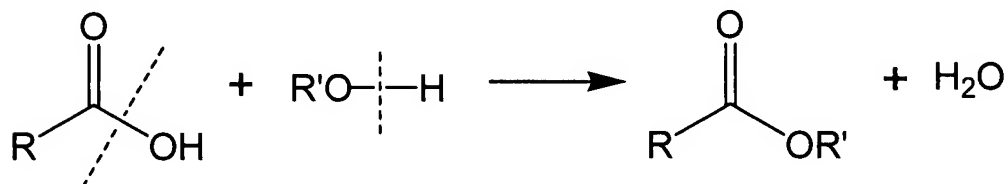
No new matter has been added.

II. FURTHER REMARKS ON THE DEFINITENESS OF CLAIMS 1-4

In the Office Action dated February 1, 2007, claims 1-4 were rejected under 35 USC 112, second paragraph, as indefinite. Such a ground of rejection was overcome in our last response as indicated in the most recent Office Action. To further expedite prosecution of this application and to assist the Examiner in examination of such, Applicants herein provide further remarks about the definiteness of this claim language.

On page 2 of the February 1, 2007 Office Action, the Office stated that "It is unclear how amino acids, or its derivatives are prepared when R⁴ can be a heterocyclic group". However, Applicants' note that it is quite clear that an optically active β -amino acid derivative of the claimed invention can be prepared when R⁴ is a heterocyclic group.

To demonstrate such, the esterification of a carboxylic acid is as shown in the following scheme:



This scheme shows that the "-OH" of the carboxylic acid is replaced by "-OR'" of the alcohol. Thus, when a carboxy group (-COOH) is esterified by the alcohol, a bond of -OH to a carbon atom of carbonyl group in the carboxy group is cleaved. For example, in peptide synthesis, a carboxy moiety is reacted (condensed) with an amino moiety to form a peptide linkage, *i.e.*;



Therefore, when R⁴ is a heterocyclic group in an optically active β -amino acid derivative of the formula (2) produced by the claimed process, the moiety of -COR⁴ can be easily converted to -COOH (*i.e.* an ester).

III. OBVIOUSNESS REJECTION

On pages 2-4 of the last Office Action, claims 1-5 and 7 were rejected under 35 U.S.C. § 103(a) as obvious over Li et al. in view of Sibi et al. (US 6,080,857). Applicants respectfully traverse this rejection, as applied to the amended claims, for the following reasons.

A. Li does not teach or suggest hydroamination in the presence of an acid, an asymmetric reaction or optically pure β -amino acid.

In amended claims 1 to 5 and 7, an α,β -unsaturated carboxylic acid derivative of formula (1) is reacted with an amine in the presence of a chiral catalyst and in the presence of an acid. On the other hand, there is neither a description nor a suggestion of "in the presence of an acid" in Li. Li therefore does not disclose or suggest hydroamination in the presence of an acid.

Further, the claimed invention is directed to a process for producing an optically active β -amino acid derivative. However, Li does not disclose an asymmetric reaction or the optical purity of the obtained β -amino acid.

For the forgoing reasons, Li fails to teach or suggest every element of the claimed invention.

B. Sibi fails to disclose that the reaction is carried out in the presence of a Lewis acid or that a Lewis acid is added to the reaction system in addition to a chiral catalyst.

Sibi describes a Lewis acid. However, Sibi describes a chiral Lewis acid complex which is prepared from $\text{MgBr}_2 \cdot \text{Et}_2\text{O}$ (Lewis acid) and a chiral bisoxazolinylmethane ligand (see column 1, lines 51-53, and EXAMPLES). Thus, Sibi discloses that the reaction is carried out NOT in the presence of a Lewis acid BUT in the presence of a chiral Lewis acid complex obtained from $\text{MgBr}_2 \cdot \text{Et}_2\text{O}$ (Lewis acid) and a chiral bisoxazolinylmethane ligand. The Lewis acid described in Sibi is merely a raw material for the complex. Further, Sibi does not disclose that a Lewis acid is added to a reaction system in addition to a chiral catalyst.

C. Sibi fails to disclose the catalyst.

As noted above, Sibi describes that the reaction is carried out in the presence of a complex which is prepared from $\text{MgBr}_2 \cdot \text{Et}_2\text{O}$ (Lewis acid) and a chiral bisoxazolinylmethane ligand. However, Sibi does not disclose the structural formula of the complex prepared from $\text{MgBr}_2 \cdot \text{Et}_2\text{O}$ and a chiral bisoxazolinylmethane ligand. It is therefore unclear what kind of substance is used as a catalyst in Sibi.

D. Sibi fails to disclose the excellent enantiomeric excess of the claimed invention.

The problem to be solved by the claimed invention is to provide a process for producing an optically active β -amino acid derivative in high yields with high optical purity. This problem has been solved by the processes for producing an optically active β -amino acid derivative according to claim 1.

Particularly, an optically active β -amino acid derivative can be produced in very high yields with high enantioselectivities by reacting an α,β -unsaturated carboxylic acid derivative with an amine in the presence of a chiral catalyst and in the presence of an acid. Thereby both excellent yields and excellent enantiomeric excess can be achieved, as shown in Examples 8 and 10 of the specification.

Example 8 discloses the reaction of anisidine with 3-crotonyl-1,3-oxazolidin-2-one in the presence of a chiral palladium catalyst and in the presence of trifluoromethanesulfonic acid. A yield of 96% and an enantiomeric excess of 94% was achieved.

Example 10 discloses the reaction of aniline with 3-crotonyl-1,3-oxazolidin-2-one in the presence of a chiral palladium catalyst and in the presence of trifluoromethanesulfonic acid. A yield of 89% and an enantiomeric excess of 94% was achieved.

On the other hand, in Sibi, even in case where the enantiomeric excess of 90% or more was achieved, the yield was at most 63% (Entry 2a on TABLE I, column 9 of Sibi).

Thus, the excellent yields in combination with excellent enantiomeric excesses of the claimed invention are neither disclosed nor suggested by Sibi. Therefore, this effect of the

claimed invention is quite unobvious from Sibi to those skilled in the art.

E. Sibi fails to disclose the process of the claimed invention which is suitable for industrial processes and has excellent workability.

In Sibi, $\text{MgBr}_2 \cdot \text{Et}_2\text{O}$ is used as a representative Lewis acid (see EXAMPLES of Sibi). Sibi describes in the EXAMPLES that the reaction is carried out in the presence of the Lewis acid complex formed from $\text{MgBr}_2 \cdot \text{Et}_2\text{O}$ and chiral bisoxazolinylmethane ligand. $\text{MgBr}_2 \cdot \text{Et}_2\text{O}$ is quite unstable and may decompose due to moisture in the atmosphere. Thus, $\text{MgBr}_2 \cdot \text{Et}_2\text{O}$ must be handled under inert gas atmosphere, resulting in increased difficulty in performing the process.

Therefore, the process disclosed in Sibi is not industrial.

On the other hand, in the claimed process, the asymmetric hydroamination is carried out both in the presence of nitrogen and in the absence of nitrogen as disclosed in Examples of the present specification. The claimed process does not always need the inert gas atmosphere condition. Thus, the claimed process is suitable for industrial processes and has an excellent workability.

F. Conclusion

For the above-noted reasons, Applicants contend that the process of claim 1 is unobvious from Li in view of Sibi to those skilled in the art. Further, since claims 2 to 5 and 7 are dependent on claim 1, the subject matter of claims 2-5 and 7 are also unobvious from Li in view of Sibi to those skilled in the art.

For the above noted reasons, Applicants respectfully suggest that this rejection, as applied to the amended claims, is untenable and should be withdrawn.

IV. ANTICIPATION REJECTION

On pages 4-5, Claim 6 was rejected under 35 U.S.C. § 102(b) as anticipated by Renzi. Applicants respectfully traverse this rejection as applied to amended claim 6.

In a compound of the formula (4b) as claimed in amended claim 6, since R¹ is not a hydrogen atom, a carbon atom attached to R¹ and R² is an asymmetric carbon atom. On the other hand, the compounds disclosed in Renzi have no asymmetric carbon atoms because both the carbon atom to which an amino group is bonded and the adjacent carbon atom have two hydrogen atoms, respectively.

Further, R^D in the claimed compound (4b) is not disclosed in Renzi. Thus, the claimed compound (4b) is quite structurally different from the compounds disclosed in Renzi. Therefore, the subject matter of amended claim 6 is not anticipated by Renzi.

Therefore, for the above-noted reasons, Applicants respectfully suggest that this rejection, as applied to amended claim 6, is untenable and should be withdrawn.

V. NEW CLAIM 8

In new claim 8, "a chiral catalyst" has been limited to "a chiral transition-metal complex of the formula (5) or of the formula (6)". The chiral transition-metal complex of the formula (5) or of the formula (6) is neither disclosed nor suggested in Sibi.

Further, Li is not a relevant prior art to the claimed invention described above. Therefore, the invention of new claim 8 is also unobvious over Li in view of Sibi.

VI. CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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